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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,000	03/13/2001	Geert Jannes	2752-33	1152

7590 09/10/2002

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EXAMINER
FOLEY, SHANON A

ART UNIT	PAPER NUMBER
1648	11

DATE MAILED: 09/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,000	JANNES ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *6-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I and specific primer set of SEQ ID NO: 18 and 19 in Paper No. 10 is acknowledged. It is noted that applicant also elected a single probe for each of the organisms listed in claim 1. As discussed in the restriction requirement, group I is drawn to a method of detecting infection by amplification with a primer set and detecting the amplified products with a probe (emphasis added). The primer set elected corresponds to *Mycoplasma pneumonia* primers according to Table 4 on page 24 of the disclosure. Therefore, the first elected probe corresponding to the product amplified by the elected primer set is SEQ ID NO: 15. The other elected probes are drawn to a non-elected invention and are withdrawn from consideration.

Applicant requests the examiner to indicate the PCT rules that allow the requirement for one primer set and one probe because the reasons providing the basis for the requirement appear to originate from US practice. Applicant argues that the limitation to specific sequences imposed by the requirement is contrary to the instant invention. Applicant further asserts that an examination of all primer pairs and probes would not pose an undue search burden because they are used for structurally and functionally related products with common target sequences. Applicant also states that detection sometimes requires the use of more than one probe.

Applicant's arguments have been fully considered, but are found unpersuasive. The specific PCT rules that allow a restriction requirement between different inventive concepts is PCT Rules 13.1 and 13.2 for considering unity of invention, see Appendix T in the MPEP. The instant claims do not maintain unity of invention because the claims do not share a

corresponding special technical feature. In the instant case, the special technical feature of group I is method steps using a primer mixture and a probe to detect an amplified product. Group II does not share the special technical feature of group I because one or more of the criteria defining the special technical feature of group I is not found in group II.

Each of the primers in Tables 2 and 4 of claim 4 and the probes used to detect amplified products in claim 5 are drawn to structurally distinct nucleotide sequences that are each used for different purposes. None of the primers or probes has the same sequence and each are designed to bind to different regions of an organism or completely unrelated organisms. Each of the primers and probes in the instant application are distinct and each has a separate specific use because none of the primers and probes can bind to the identical nucleotide sequence. Therefore, each of the primers and probes represent a separate product and process of using the product, which lacks unity of invention under 37 CFR § 1.475, see Appendix R of the MPEP.

It should be noted that there is no requirement for establishing burden of search in national stage applications filed under 371 for determining lack of unity between inventions. However, in response to applicant's arguments regarding search burden, the instant case would pose a serious burden for the Office if all of the primers and probes were rejoined. A divergent and non-overlapping search would be required because each SEQ ID NO. must be searched independently of all others in patent and non-patent literature databases world-wide, which uses the time and resources of the Office as there are only two sequence processors in the entire technology center.

Applicant should also note that examination of the elected group is not limited in view of the required sequence election because the claims of group I will be examined in their broadest possible interpretation.

The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 6-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10. Claims 1-5 and SEQ ID NOs: 18, 19, and 15 are under consideration.

Information Disclosure Statement

The information disclosure statement filed March 13, 2001 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language, i.e. DE 197 16 456. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

Claim 3 is objected to because of the following informalities: "wherein in addition also" is awkward.

Claim 4 is objected to because of the following informalities: "of" is presumably "or". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step in claim 1 is: a mechanism for detecting the products amplified by the primer mixture. There is no detection step to determine which sequences are amplified in claim 1. In addition, it appears that claim 1 is drawn to a detection method for respiratory tract infections by amplifying sequences that are already present in a sample. If it is known that the sample contains the sequences, what is the object of the method? It is suggested that "may be" be inserted before "present". Also, the word "means" appears to be used to indicate a specified function. However, since no function is specified by the word(s) preceding "means," it is impossible to determine the equivalents of the element, as required by 35 U.S.C. 112, sixth paragraph. See *Ex parte Klumb*, 159 USPQ 694 (Bd. App. 1967).

Claim 2 is unclear. The claim states that the 16S rRNA primers of claim 1 are "replaced by primers from the spacer region between the 16S and the 23SrRNA sequences". It cannot be discerned how the primers of claim 1 are "replaced". Does this mean that the 16S rRNA primers are not used in the method of claim 1 and other primers are used instead? Or, are the replacement primers used in addition to the 16S rRNA primers after amplification takes place? It is also unclear what the phrase, "primers from the spacer region between the 16S and the 23S rRNA sequences" is referring to. Is this the region amplified by the 16S rRNA primers or the

primers that are replacing them? It is unclear what the "spacer region" between 16S and 23S rRNA is. The 16S rRNA sites in claim 1 are derived from *M. pneumoniae* and *C. pneumoniae*. Is the spacer region between the 16S and the 23S rRNAre also derived from these organisms?

It is presumed that the primers of claim 3 are used to amplify sequences from the specified organisms and not for direct detection since there is no mechanism in the primers that would convey the presence of the organisms. There is also no indication for how these primers are used.

Claims 4 and 5 are vague and indefinite for referring to the Tables in the specification. The claims do not clearly define which specific primers are being claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jannes et al. (US 6,025,132), Claas et al. (Journal of Virological Methods. 1992; 39 (1-2) 1-13, abstract only), Paton et al. (Journal of Clinical Microbiology. 1992; 30 (4): 901-904, abstract only), Kinchington et al. (Investigative Ophthalmology and Visual Science. 1994; 35 (12): 4126-34, abstract only), Saikku et al. (Clinical Microbiol and Infect. 1997; 3 (6): 599-606), Gilbert et al. (Journal of Clinical Microbiology. 1996; 34 (1): 140-143), Fluitt et al. (WO 95/13396. May, 1995; GenEmbl Accession No: A44457), Jannes et al. (WO 96/00298. January, 1996; GenEmbl

Accession No: A47982), and Echevarria et al. (Journal of Clinical Microbiology. May, 1998; 36 (5): 1388-1391).

The claims are drawn to a method of detecting acute respiratory tract infections in a sample by simultaneous amplification of specific genes of various bacteria and viruses with at least one primer set for each gene to be amplified and subsequently detecting amplified sequences with a probe specific for each of the amplified products.

Saikku et al. teaches that respiratory tract infections are caused by influenza A and B, adenovirus, parainfluenza viruses, respiratory syncytial viruses, enteroviruses, *M. pneumonia*, and *C. pneumonia*, see Table 1 on page 599. Saikku et al. also teaches that nucleic acid detection methods to diagnose respiratory diseases provide sensitive and specific diagnosis within 24 hours, see the last paragraph before the "Treatment" section on page 602.

Saikku et al. does not teach simultaneous amplification of all of the nucleic acids from the pathogens that might be present in a sample or specific primers and probes to the specific regions claimed.

Gilbert et al. teaches simultaneous amplification and probe detection with several different primer sets of clinical samples by RT-PCR to determine whether a patient is infected with respiratory syncytial virus, parainfluenza virus, and picornaviruses, see the abstract and the materials and methods section. To determine whether a patient has PIV-3 or an enterovirus, Gilbert et al. amplifies the 5' non-coding region of the PIV-3 fusion protein gene and the 5' non-coding region of an enterovirus, see "RT-PCR" bridging columns on page 140. Gilbert et al. does not teach specifically detecting the regions for influenza virus A or B, hemagglutininneuraminidase gene for PIV-1, the F1 subunit of the fusion protein of RSV, or

detecting the instant regions for *M. pneumonia* and *C. pneumonia* or *B. pertusis* and *B. parapertusis*.

However, Claas et al. teaches detecting a PCR technique for simultaneous type-specific identification of influenza virus A and B using a combination of primer sets specific for the non-structural proteins of the viruses, see the abstract provided. This reference is admitted prior art on page 13, lines 14-25.

Paton et al. teaches specific detection of respiratory syncytial virus in clinical samples by PCR amplifying the F1 subunit of the fusion protein of RSV, see the abstract provided. This reference is admitted prior art on page 13, lines 14-25.

Echeverria et al. teaches the simultaneous PCR amplification and probe detection of clinical samples to determine if the sample contains PIV-1, PIV-2, or PIV-3 using a primer mixture and amplifies the hemagglutininneuraminidase gene for PIV-1, see the materials and methods section.

Kinchington et al. (Investigative Ophthalmology and Visual Science. 1994; 35 (12): 4126-34, abstract only) teaches specific amplification and probe detection of the adenovirus hexon gene in clinical samples using PCR, se the abstract provided.

Jannes et al. teaches the simultaneous PCR amplification and probe detection of microorganisms in a respiratory tract infection sample, see claim 1. Jannes et al. also teaches specific primers and probes to amplify and detect the 16S rRNA sequence, the spacer region between the 16S and the 23S rRNA sequence of *M. pneumonia* and *C. pneumonia* and also teaches the specific detection of *B. pertusis* and *B. parapertusis*, see the table of column 13,

column 18, lines 44-54, column 38, line 42 to column 40, line 22, and Example 6 in column 62, line 71 to column 63, line 62.

SEQ ID NO: 15 and 18 are taught by Fluitt et al. and Jannes et al. WO 96/00298, respectively.

One of ordinary skill in the art at the time the invention was made would have been motivated to simultaneously detect respiratory tract disease organisms and viruses to more quickly determine the pathologic cause of the disease to administer the proper treatment as soon as possible. Saikku et al. teaches that there are no symptoms that readily differentiate the pathogen causing the respiratory infection, see the last paragraph on page 600. Therefore, simultaneous detection of multiple organisms would eliminate improper diagnosis and treatment because specific identification of the pathogen(s) causing the infection would be known. One of ordinary skill in the art at the time the invention was made would have been further motivated to PCR amplify respiratory tract infections because the method is less time consuming than culturing swabs from the respiratory tract of an infected individual and because PCR is a sensitive and specific technique. Gilbert et al. teaches that the PCR method had over 94% sensitivity for detecting the different viruses. One of ordinary skill in the art at the time the invention was made would have combined the specific primers and probes to amplify the instant regions taught by Claas et al., Jannes et al., Paton et al., Echeverria et al., Fluitt et al., Jannes et al. WO 96/00298, Kinchington et al., and Gilbert et al. because each reference teaches a specific region unique to the virus or bacteria detected. This ensures that there is no mistaken identity for each of the products amplified and subsequently detected by a probe specific for each amplified product. One of ordinary skill in the art at the time the invention was made would have had a

reasonable expectation for producing combining the primers taught by the references to detect multiple respiratory tract pathogens because each of the references demonstrate that the specific primers and probes taught are highly specific for the pathogen to be amplified against control samples. Also, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for screening for multiple organisms taught because Jannes et al., Echeverria et al., and Gilbert et al. teach the simultaneous identification of various pathogens using multiplex PCR techniques and Gilbert et al. teaches that the PCR diagnostic panel is easily expanded to include other pathogens, see the discussion section on page 142, which would include the specific primers and probes of Claas et al., Paton et al., Jannes et al. WO 96/00298, Fluitt et al., and Kinchington et al. to readily differentiate the pathogen causing the respiratory infection taught by Saikku et al. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Allowable Subject Matter

The prior art does not teach or suggest SEQ ID NO: 19.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley
September 6, 2002

JAMES HOUSEL 9/9/02
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600